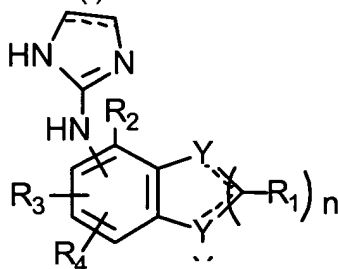


212 consisting of hydrogen, halogen, lower alkyl and lower alkenyl; n is an integer from 1 to 3; and a broken line beside a solid line indicates a single or double bond, provided that two double bonds are not on the same carbon in the case when n=1.

A3 21) (Amended) A method of preventing degeneration of the optic nerve and providing protection of the retinal ganglion cells of a mammal, comprising administering to the mammal a therapeutically effective amount of a prostaglandin and a therapeutically effective amount of an alpha adrenergic agent of formula (I)



formula (I)

wherein each Y is independently selected from the group consisting of N, N-CH<sub>3</sub>, O, S and C-  
R<sub>1</sub>; R<sub>1</sub> is hydrogen, lower alkyl or oxo; R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> are independently selected from the group consisting of hydrogen, halogen, lower alkyl and lower alkenyl; n is an integer from 1 to 3; and a broken line beside a solid line indicates either a single or a double bond, provided that two double bonds are not on the same carbon in the case when n=1, and their pharmaceutically acceptable salts and esters as appropriate.

#### REMARKS

The present amendments involve the cancellation of claims 7-13 and amendment of claims 1, 14, and 21. The amendments to claim 1 merely moves a preamble limitation to the body of the claim. The amendment to claim 14 adds the requirement that the claimed article comprise a composition useful for neuroprotection. This amendment is supported by originally filed claim 1 and the specification. Finally, the amendment to claim 21 removes unnecessary claim language. None of these amendments narrow the claims or add new matter.

No fee is thought due in connection with the filing of this Preliminary Amendment. However, if Applicant is in error, kindly use our Deposit Account No. 01-0885.

Docket No. 17095CIPCON(AP)  
Garst, M.

PATENT

Respectfully submitted,

Dated: 7/11/01

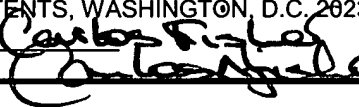
By: 

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CERTIFICATE OF MAILING

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES  
POSTAL SERVICE AS EXPRESS MAIL NO. EL38533767 ADDRESSED TO: BOX PATENT APPLICATION,  
ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231 ON 7/12/01

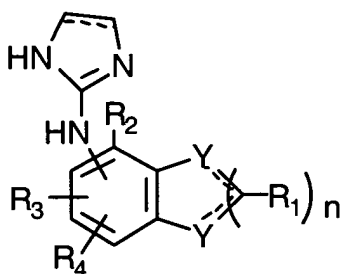
Printed name of Person Making Deposit: Carlos A. Fisher

Signature of Person Making Deposit: 

Date: 7/11/01

MARKED-UP AMENDED CLAIMS

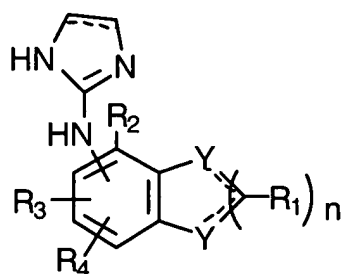
1) (Amended) A topical ophthalmic composition useful for controlling elevated intraocular pressure associated with glaucoma and ocular hypertension while providing neuroprotection to the ocular nerves, comprising a combination of a therapeutically effective amount of a prostaglandin and a therapeutically effective amount of an alpha adrenergic agent of formula (I)



formula (I)

wherein each Y is independently selected from the group consisting of N, N-CH<sub>3</sub>, O, S and C-R<sub>1</sub>; R<sub>1</sub> is hydrogen, lower alkyl or oxo; R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> are independently selected from the group consisting of hydrogen, halogen, lower alkyl and lower alkenyl; n is an integer from 1 to 3; and a broken line beside a solid line indicates a single or double bond, provided that two double bonds are not on the same carbon in the case when n=1, and their pharmaceutically acceptable salts and esters as appropriate, wherein said composition lowers intraocular pressure and provides neuroprotection.

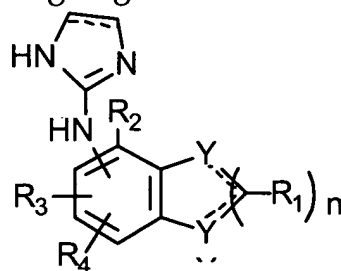
14) (Amended) An article of manufacture comprising packaging material and a pharmaceutical combination [of] comprising at least one alpha adrenergic agent and at least one prostaglandin and their pharmaceutically acceptable salts and esters as appropriate [contained within said packaging material], wherein the pharmaceutical agents are effective in controlling elevated intraocular pressure associated with glaucoma and ocular hypertension and providing neuroprotection, and wherein the packaging material comprises a label which indicates that said combination can be used for control of elevated intraocular pressure or in treating glaucoma, and wherein said alpha adrenergic agent is represented by formula (I)



formula (I)

wherein each Y is independently selected from the group consisting of N, N-CH<sub>3</sub>, O, S and C-R<sub>1</sub>; R<sub>1</sub> is hydrogen, lower alkyl or oxo; R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> are independently selected from the group consisting of hydrogen, halogen, lower alkyl and lower alkenyl; n is an integer from 1 to 3; and a broken line beside a solid line indicates a single or double bond, provided that two double bonds are not on the same carbon in the case when n=1.

21) (Amended) A method of preventing degeneration of the optic nerve and providing protection of the retinal ganglion cells of a mammal [suffering from glaucoma or ocular hypertension], comprising administering to the mammal a therapeutically effective amount of a prostaglandin and a therapeutically effective amount of an alpha adrenergic agent of formula (I)



formula (I)

wherein each Y is independently selected from the group consisting of N, N-CH<sub>3</sub>, O, S and C-R<sub>1</sub>; R<sub>1</sub> is hydrogen, lower alkyl or oxo; R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> are independently selected from the group consisting of hydrogen, halogen, lower alkyl and lower alkenyl; n is an integer from 1 to 3; and a broken line beside a solid line indicates either a single or a double bond, provided that two double bonds are not on the same carbon in the case when n=1, and their pharmaceutically acceptable salts and esters as appropriate.